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Phrenic Nerve Injury After Atrial Fibrillation Catheter Ablation

Characterization and Outcome in a Multicenter Study

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OBJECTIVES The purpose of this study was to characterize the occurrence of phrenic nerve injury (PNI) and its outcome after radiofrequency (RF) ablation of atrial fibrillation (AF).

BACKGROUND It is recognized that extra-myocardial damage may develop owing to penetration of ablative energy.

METHODS Between 1997 and 2004, 3,755 consecutive patients underwent AF ablation at five centers. Among them, 18 patients (0.48%; 9 male, 54 ± 10 years) had PNI (16 right, 2 left). The procedure consisted of pulmonary vein (PV) isolation in 15 patients and anatomic circumferential ablation in 3 patients, with additional left atrial lesions (n = 11) and/or superior vena cava (SVC) disconnection (n = 4).

RESULTS Right PNI occurred during ablation of right superior PV (n = 12) or SVC disconnection (n = 3). Left PNI occurred during ablation at the left atrial appendage. Immediate features were dyspnea, cough, hiccup, and/or sudden diaphragmatic elevation in 9, and in the remaining the diagnosis was made after ablation owing to dyspnea (n = 7) or on routine radiographic evaluation (n = 2). Four patients (22%) were asymptomatic. Complete recovery occurred in 12 patients (66%). Recovery occurred within 24 h in the two patients with left PNI and in one patient with right PNI occurring with SVC disconnection. In the other nine patients, right PNI recovery occurred after 4 ± 5 months (1 to 12 months) with respiratory rehabilitation. After a mean follow-up of 36 ± 33 months, six patients have persistent PNI (three with partial and three with no recovery).

CONCLUSIONS In this multicenter experience, PNI was a rare complication (0.48%) of AF ablation. Ablation of the right superior PV, SVC, and left atrial appendage were associated with PNI. Complete (66%) or partial (17%) recovery was observed in the majority. (J Am Coll Cardiol 2006;47: 2498–503) © 2006 by the American College of Cardiology Foundation

Catheter ablation of drug-refractory atrial fibrillation (AF) is increasingly used. As with all evolving techniques, unexpected complications may occur. Some of them are now well known: pericardial effusion (1), stroke (2), and pulmonary vein (PV) stenosis (3). The recent descriptions of atrio-esophageal fistula (4) and gastric hypomotility (5) have highlighted the potential for extracardiac penetration of ablative energy. Few cases of phrenic nerve injury (PNI) have been reported after catheter ablation (6–8). This study characterizes a multicenter experience of the occurrence and outcome of PNI during the catheter ablation of AF.

METHODS

Study population. Consecutive patients who developed PNI during catheter ablation of drug-refractory paroxysmal, persistent, or permanent AF at the five centers between 1997 and 2004 were included. During this period, 3,755 patients underwent AF ablation at these centers. All patients provided written informed consent for their ablation procedure.

Ablation procedure. The ablation procedure performed in this cohort varied as the strategy of ablation evolved over the period studied. In general, before 2000, focal ablation or segmental pulmonary vein (PV) ablation was performed. However, after 2000, different strategies have been used based on incorporating a variable component of atrial tissue surrounding the PV with or without the end point of complete isolation. Depending on AF type, inducibility and/or AF recurrence, linear atrial lesions, and/or superior vena cava (SVC) disconnection, ablation of extra PV foci were performed. Radiofrequency (RF) energy was used in all but one patient, in whom ultrasound energy was used exclusively for PV ablation. Different ablation catheters were also used: conventional 4-mm-tip, 8-mm-tip, 4-mm irrigated tip catheter, or balloon for ultrasound. Generator settings were dependent on the catheter tip. The temperature target was limited to 48°C and the maximum power output varied from 30 to 45 W in the atria and 30 W at the PV ostia for the irrigated tip;

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Abbreviations and Acronyms

AF = atrial fibrillation
LIPV = left inferior pulmonary vein
PN = phrenic nerve
PNI = phrenic nerve injury
PV = pulmonary vein
RF = radiofrequency
RSPV = right superior pulmonary vein
SVC = superior vena cava

60°C and 60 W were used with the 8-mm-tip catheter; and 65°C and 40 W were used with the ultrasound balloon.

Data collection and follow-up. Baseline clinical and procedural data were collected retrospectively. Every patient had a chest X-ray before the procedure. During the procedure, diaphragmatic movements were monitored by fluoroscopy. Follow-up was performed in consultation or short hospitalization at 1, 3, 6, 9, and 12 months after the procedure. Data from clinical evaluation, Holter electrocardiogram, transthoracic echocardiography, treadmill test, and computerized tomography of the pulmonary vein were systematically collected. Diaphragmatic palsy due to PNI was defined as hemidiaphragmatic elevation with paradoxic movement during inspiration. When the diagnosis was confirmed, they had inspiration and expiration chest X-ray repeated at 1, 3, 6, and 12 months. Complete recovery was defined by normal diaphragmatic movement without hemidiaphragm elevation. Partial recovery was considered in the absence of paradoxic movement with a hemidiaphragm less elevated than after the procedure.

Statistical methods. Continuous variables are reported as mean ± SD. The Kruskall-Wallis test was used for comparison of variables. A p value of <0.05 was considered to be significant.

RESULTS

Patient characteristics. Eighteen patients (age 54 ± 10 years, 9 male) had a PNI out of 3,755 consecutive AF ablation procedures (prevalence 0.48%, range 0.37% to 1.6% at the different institutions). They had paroxysmal AF (n = 10) for 58 ± 46 months or sustained persistent/permanent AF (n = 8) for 8 ± 5 months and had failed 3 ± 1 antiarrhythmic drugs. Three patients had a dilated cardiomyopathy with a mean left ventricular ejection fraction of 39 ± 8%, one had hypertrophic cardiomyopathy, and two had pulmonary disease (chronic bronchopneumopathy and pulmonary fibrosis after amiodarone use).

Catheter ablation (Table 1). A total of 21 ablation procedures were performed in the 18 patients before PNI (1 in 15 patients and 2 in 3 patients). All four PV were disconnected in 14 patients, whereas in one (Patient #17) only three PV were targeted. Three patients had a wide anatomic

Table 1. Patients and Procedure Characteristics

Patient	Gender	Age (yrs)	AF Type	Procedure	Type of Energy	Catheter Tip	Power on RSPV (W)	Temperature Max on RSPV (°C)
1	Male	57	Paroxysmal	PVI	RF	4 mm	—	—
2	Female	61	Paroxysmal	PVI + MI	RF	Irrigated 4 mm	30	48
3	Male	55	Permanent	PVI + post. LA isolation + MI	RF	Irrigated 4 mm	30	48
4	Male	47	Paroxysmal	WACA + MI	RF	8 mm	60	60
5	Female	62	Paroxysmal	WACA + RI-MVA + roof + SVC disconnection	RF	4 mm	48	—
6	Male	47	Persistent	WACA + roof + MI	RF	8 mm	—	—
7	Male	49	Permanent	PVI + roof + MI + defragmentation + SVC disconnection	RF	Irrigated 4 mm	30	48
8	Female	54	Paroxysmal	PVI + roof + foci	RF	Irrigated 4 mm	30	48
9	Male	67	Permanent	PVI + post. LA isolation + foci	RF	Irrigated 4 mm	30	48
10	Female	36	Permanent	PVI + post. LA isolation + MI + SVC disconnection	RF	Irrigated 4 mm	30	48
11	Male	58	Paroxysmal	PVI	Ultrasound	Balloon	40	64
12	Female	62	Permanent	PVI + MI + roof + SVC disconnection	RF	Irrigated 4 mm	30	48
13	Male	39	Permanent	PVI + MI	RF	Irrigated 4 mm	41	48
14	Female	67	Paroxysmal	PVI	RF	8 mm	30	50
15	Female	50	Paroxysmal	PVI	RF	Irrigated 4 mm	30	50
16	Female	56	Paroxysmal	PVI	RF	Irrigated 4 mm	30	48
17	Female	72	Paroxysmal	PVI except RIPV	RF	4 mm	30	—
18	Male	41	Permanent	PVI	RF	Irrigated 4 mm	30	50
Totals	9 Male 9 Female	54 ± 10	10 Paroxysmal 8 Persistent/Permanent	15 PVI 3 WACA 4 SVC disconnection	17 RF 1 US	11 Irrigated tip 3 8-mm tip 3 4-mm tip	35 ± 9 W	51 ± 5°C

AF = atrial librillation; MI = mitral isthmus line between mitral annulus to left inferior pulmonary vein; PVI = all pulmonary veins isolation; post. LA isolation = posterior left atrial isolation; RF = radiofrequency; RI-MVA = line between right inferior pulmonary vein and mitral annulus; SVC = superior vena cava; WACA = wide anatomic circumferential ablation.

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circumferential ablation. Left atrial linear ablation was performed in 11 patients. This included mitral isthmus ablation (n = 8; linear lesion between mitral valve annulus and left inferior pulmonary vein [LIPV]), roof line (n = 5; linear lesion between the two superior PV), posterior left atrial isolation (n = 3; linear lesions joining the four PV), and/or a linear lesion between the right inferior PV and the mitral annulus (n = 1). In two patients, non-PV foci were localized and ablated at the left atrial appendage roof. Four patients had SVC disconnection. None underwent right atrial linear lesions other than cavotricuspid isthmus ablation.

PNI (Table 2). Sixteen patients had right and two developed left PNI (Patients #8 and #9). The diagnosis was made during the procedure for nine, including the two patients with left PNI. The onset of PNI was heralded during ablation by dyspnea, cough, or hiccup in seven. However, two patients were asymptomatic. Three of these nine (Patients #1, #3, and #17) had the diagnosis of right PNI made during right superior pulmonary vein (RSPV) isolation (anteroinferior part), three (Patients #7, #10, and #12) during SVC disconnection (posteroseptal part), and one (Patient #11) before any energy delivery, the latter attributed to internal jugular catheterization. The two left PNI occurred during ablation of foci at the roof of the left atrial appendage.

In the nine remaining patients, the diagnosis of PNI was made immediately after the procedure (up to three days) owing to dyspnea especially while lying down (n = 7), chest pain (n = 1), atelectasis (n = 1), pleural effusion (n = 2) and/or pulmonary infection (n = 3). Two patients had no symptoms, and PNI was recognized on a routine chest X-ray after the procedure. One of these nine patients had SVC disconnection, and none had right atrial linear lesions. In these patients, PNI was presumably attributed to right PV isolation. Patients with right PNI due to right PV isolation had a mean RF time of 16 ± 7 min on right PV. Asymptomatic PNI occurred in 22% (4 of 18).

Outcome (Table 2). After a mean follow-up of 36 ± 33 months (median 22 months, range 6 to 106 months), twelve patients had complete recovery (Fig. 1), three had partial recovery, and three had no recovery of diaphragmatic function. Complete recovery occurred 4 ± 5 months after the index procedure (range 1 day to 12 months). The patient with PNI before RF delivery (Patient #11) was excluded from the above and made a complete recovery after 19 months. In the nine patients with the diagnosis of PNI made during the procedure, complete recovery of PNI was observed within 24 h for three patients (Patients #8 and #9 with left PNI and Patient #10 with right PNI after SVC disconnection). In all three cases, the diagnosis was made during the procedure with early interruption of RF. In the nine remaining patients diaphragmatic function recovered with respiratory rehabilitation during follow-up. Patients in whom the diagnosis of PNI was made during the procedure had a shorter recovery time compared with those in whom the diagnosis was made after the procedure: 2 ± 3 months (median 1.5 months) versus 7 ± 5 months (median 6 months), respectively ($p = 0.027$).

Three patients had partial recovery after 8 ± 5 months, two with persistent dyspnea especially in the supine posture and the other asymptomatic. None of these patients had the diagnosis made during the procedure.

Three patients had not recovered after 6, 18, and 96 months (Patients #16, #17, and #18, respectively) and remained symptomatic with dyspnea. One of these had the

Table 2. Outcome and Characteristics of PNI

Patient	Outcome	Side	Clinical Features	Time of Diagnosis	Delay to Recovery
1	Complete recovery, AF free	Right	Dyspnea, pulmonary infection	During RSPV isolation	12 months
2	Complete recovery, AF free	Right	Dyspnea	Immediately after procedure	12 months
3	Complete recovery, AF free	Right	Dyspnea, pulmonary infection	During RSPV isolation	7 months
4	Complete recovery, AF free	Right	Dyspnea	Immediately after procedure	4 months
5	Complete recovery, AF free	Right	None on systematic chest X-ray	After procedure	12 days
6	Complete recovery, AF free	Right	Dyspnea	After procedure	4 months
7	Complete recovery, AF free	Right	Dyspnea	During SVC disconnection	3 months
8	Complete recovery, AF free	Left	None on fluoroscopy	During LAA foci ablation	1 day
9	Complete recovery, AF free	Left	Dyspnea, hiccup	During LAA foci ablation	1 day
10	Complete recovery, AF recurrence	Right	None on fluoroscopy	During SVC disconnection	1 day
11	Complete recovery, AF recurrence	Right	Dyspnea on fluoroscopy	Before energy delivery	19 months
12	Complete recovery, AF recurrence	Right	Dyspnea and pleural effusion	During SVC disconnection	6 months
13	Partial recovery, AF free	Right	None on systematic chest X-ray	After procedure	6 months
14	Partial recovery, AF free	Right	Dyspnea, pleural effusion, atelectasis, and fever	Immediately after procedure	13 months
15	Partial recovery, AF recurrence	Right	Dyspnea on exertion	Immediately after procedure	6 months
16	No recovery, AF free	Right	Dyspnea	Immediately after procedure	—
17	No recovery, AF free	Right	Cough and dyspnea	During RSPV isolation	—
18	No recovery, AF recurrence	Right	Thoracic pain and dyspnea	2 Days after procedure	—
Totals	12 Complete recovery 3 Partial recovery 3 No recovery	16 Right 2 Left	4 None 14 Dyspnea	9 During procedure 5 Immediately after procedure 4 Later	6 ± 6 months

Abbreviations as in Table 1.

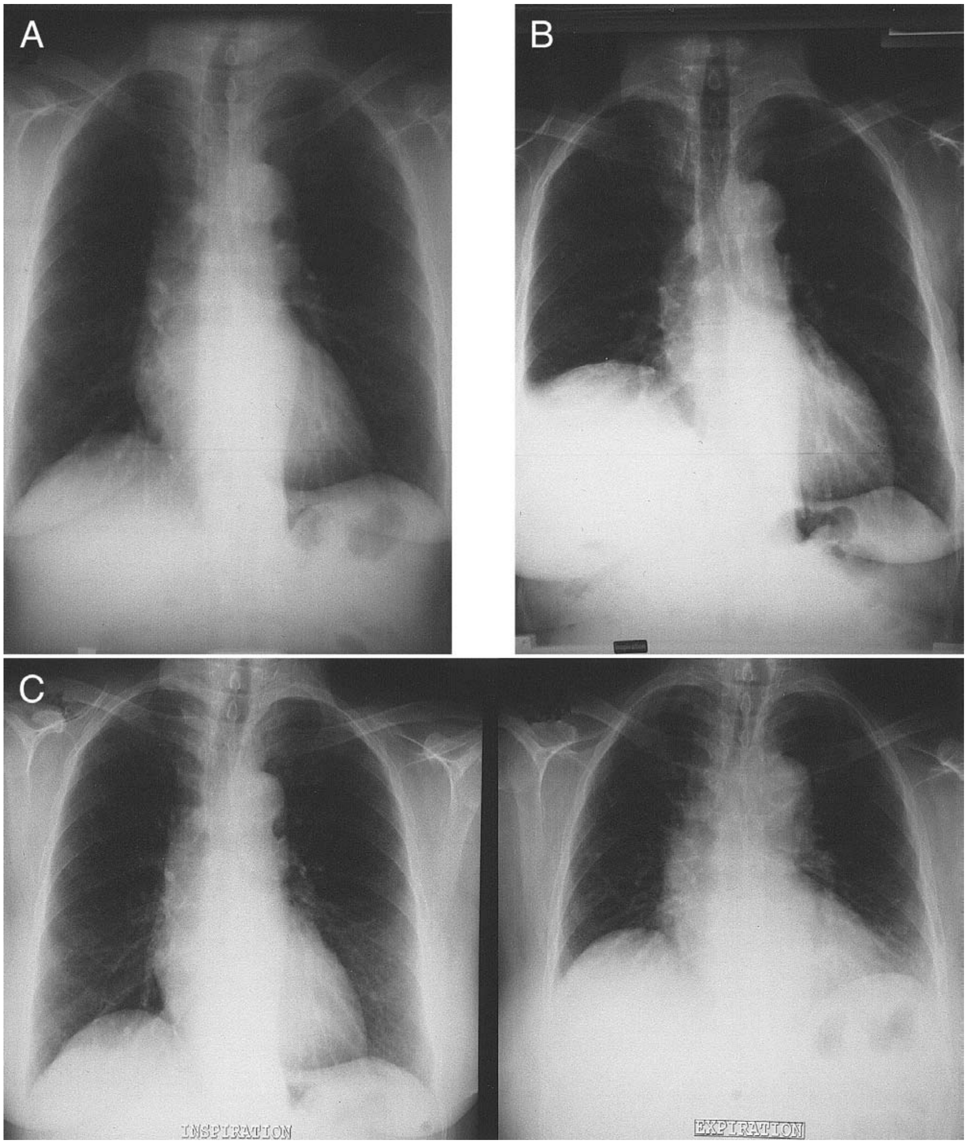

Figure 1. Chest X-ray during inspiration before ablation **(A)**, just after ablation with right phrenic nerve injury **(B)**, and one year after ablation in inspiration **(C, left)** and expiration **(C, right)**.

diagnosis made during the procedure. None of the procedural variables (power, temperature used, RF delivery time) were greater or longer ablating the RSPV than for the others. Two patients have had no AF recurrence and are symptomatically better than before the ablation. One patient had persistent limiting dyspnea and underwent plication of the right diaphragm 18 months after the development of PNI, resulting in some symptomatic improvement associated with restored right lung volume but persistent diaphragmatic paresis.

DISCUSSION

Major findings. This study reports the prevalence, severity, and long-term follow-up of PNI in the context of AF ablation. Several points need to be emphasized. 1) The prevalence of PNI in the context of AF ablation is low (0.48%). 2) No patients in this series had both right and left PNI, which would be a potentially lethal complication, but it should be considered in patients who complain from dyspnea after RF ablation. 3) Ablation of some structures is more likely to be associated with PNI and warrants greater caution during ablation (Figs. 2 and 3); these include the inferoanterior part of right PV ostium (9 to 10 o'clock), the posteroseptal part of the SVC, and the proximal left atrial appendage roof. 4) Early recognition of PNI during RF delivery allows the immediate interruption of the application which is associated with the rapid recovery of phrenic nerve (PN) function in 56%. Finally, this complication has been observed with a variety of catheters (4-mm, 8-mm, irrigated tip) and energies, suggesting that only physician "vigilance" may minimize the risk of irreversible PNI.

Anatomic sites prone to PNI. The ablation site responsible for right PNI is often the RSPV owing to its close

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Figure 2. Anatomic relationship between right phrenic nerve and heart **(left)** and left phrenic nerve and heart **(right)**. 1 = right superior pulmonary vein; 2 = right inferior pulmonary vein; 3 = left atrial appendage. Figure is courtesy of Dr. Yen Ho (Royal Brompton Hospital).

relationship with the right PN (Fig. 2). The reason some patients develop this complication and others do not remains unclear. Variable anatomy seems more probable than excessive RF delivery, which did not differ among patients. Sanchez-Quintana et al. (9) described the close relationship between the atrial tissue surrounding the RSPV at its inferoanterior area, the RSPV, and the SVC with the right PN. The RSPV and the SVC have distances varying from 1.5 to 4.5 mm and 0 to 2.3 mm, respectively, from the right PN.

Our study is the first to report left PNI during AF ablation owing to application of RF energy next to the roof of the left atrial appendage (Figs. 2 and 3). Interestingly, the two patients with left PNI recovered within 24 h, probably owing to early recognition and termination of RF delivery and the longer distance between the endocardial site of RF and left PN. Patient #10 also recovered within 24 h. She had right PNI during SVC disconnection with early termination of RF delivery. Because transient nerve effects occur before permanent damage (10) and because of the potential risk during ablation at these spots, electrophysiologists should pay particular attention to visualizing diaphragmatic excursion to anticipate PNI. In addition, before ablation of the SVC or at the roof of the left atrial appendage, pacing at the maximum output should be considered. In case of diaphragmatic contraction, RF delivery at these sites should be avoided.

Previous studies with PNI. Cardiac surgeons have studied PNI for years. It is a well known complication of myocardial

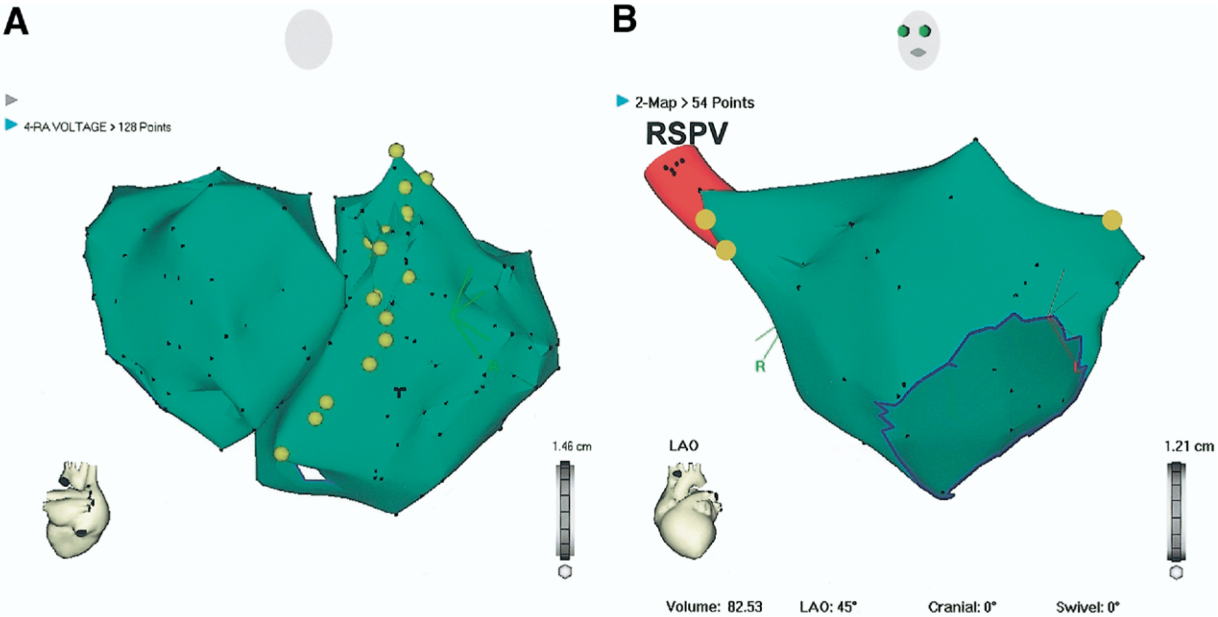

Figure 3. Endocardial site where phrenic nerve was captured in patients with phrenic nerve injury who had a redo procedure and completely recovered. **(A)** Endocardial right phrenic nerve course in the right atrium (RA) (Patient #12; posteroanterior view on anatomic Carto map). **(B)** Site where right and left phrenic nerve were captured in the left atrium (Patient #8; left anterior oblique [LAO] view on anatomic Carto map). RSPV = right superior pulmonary vein.

hypothermia during cardioplegic arrest. Studies have identified ice slush as a risk factor for PNI (11). With protective measures, the incidence of PNI decreased from 30% to 55% (11) during the early 1980s to 10% in the last few years (12). During cardiac surgery, the left PN is more often injured, because of irrigating fluid directed toward it. Recovery was observed in 72% (13) to 90% (11) of cases.

The occurrence of PNI during catheter ablation has been limited to case reports. The first report (6) describes a left PNI after ablation of a left posterolateral accessory pathway that required 39 RF applications with an 8-mm-tip catheter. The main symptom was shortness of breath, especially in the supine posture. Chest fluoroscopy showed a paresis of the left diaphragm without any paradoxic movement. At one year, left PNI function recovered and the patient became asymptomatic. Right PNI has been reported after inappropriate sinus node tachycardia ablation (7). That patient did not experience cough, hiccup, or diaphragmatic stimulation during the procedure but had shortness of breath and mild chest pain afterward. Although the patient experienced some improvement during the following months, she still remained symptomatic with persistent diaphragmatic paralysis. The last case reports a right PNI after RSPV disconnection (8) with complete recovery after four days. As in the previous case (6), a large number of RF applications ($n = 24$) had to be delivered in order to achieve RSPV disconnection.

Potential mechanisms of PNI. Several mechanisms have been proposed to explain PNI after catheter ablation: 1) direct heat transfer (14) from the ablation site to the nerve; 2) electromagnetic field generated at the catheter tip (15); and 3) generation of a resonance current around the heart (16). Bunch et al. (10) show that relatively low tissue temperature increment injures the phrenic nerve. They also point out the role of electric current on immediate nerve dysfunction. The use of a different source of energy is unlikely to prevent this complication; PNI have already been reported with cryothermia (17,18) and ultrasound (19).

Study limitations. The present study is a retrospective analysis of consecutive patients referred for AF ablation. Because of the study design, the incidence of transient asymptomatic PNI may have been underestimated.

Conclusions. In this multicenter experience, PNI was observed to be a rare complication (0.48%) of AF ablation, but it can occur particularly when targeting the right PV, the SVC, and the left atrial appendage. Complete (66%) or partial (17%) recovery of diaphragmatic function was observed in most patients.

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